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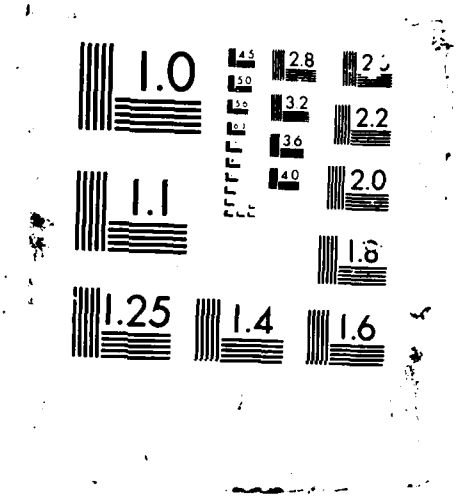
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CHEMOTHERAPEUTIC STUDIES ON SCHISTOSOMIASIS AND CLINICAL, EPIDEMIOLOGICAL AND IMMUNOLOGICAL STUDIES ON MALARIA IN AMAZONAS, BRAZIL, ALONG THE ITUXI RIVER

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During the reporting period, 457 compounds were screened in the PCT and PMT. Of these 5 were designated confirmed or unconfirmed active and 23 were toxic. Nine compounds were tested in the SCT. Upgrading of research mouse colony facilities was begun. Mark and release studies of Anopheles darlingi at the Ituxi River Study Area are being conducted to determine dispersal patterns from possible larval breeding sites. Construction of an insectary is nearing completion at the University of Brasilia. Preliminary studies to Colonize An. darlingi have been initiated.

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PROBLEMS AND OBJECTIVES:

1. Schistosomiasis and malaria continue to be two of the major health problems facing many developing countries in South America, the Carribean, Africa, the Middle East and the Far East, and pose disease threats to American personnel stationed in these areas. There is currently no single drug which presents a totally satisfactory treatment for schistosomiasis. The USAMRU-Brasilia antischistosomal drug testing program is oriented to identifying compounds or classes of compounds which elicit prophylactic and curative activity against laboratory Schistosoma mansoni infections in the rodent model.

2. Malaria in the state of Amazonas, Brazil, has become increasingly difficult to control. Plasmodium falciparum, malignant tertain malaria, has become resistant to chloroquine, sulfametoxozol and trimethoprim, sulfadoxine and pyrimethamine and other drugs. Plasmodium vivax, beign tertain malaria, is increasing even though chloroquine remains effective in the treatment and chemo-prophylaxis against it. Current control measures for suspected Anopheles vectors involve the use of the residual insecticide DDT on the inner wall surfaces of houses at 6-month intervals. Adult female An. darlingi mosquitoes, the primary vectors of malaria in Brazil, appear to avoid DDT treated surfaces of houses. Therefore the applied insecticide appears to be effective as a repellent. One objective for this year was to continue with observations of behavioral resistance of An. darlingi to entry of treated houses, while at the same time to study the potential mosquito killing capability of these same DDT treated surfaces.

Other objectives were to prepare an insectary in the Center for Tropical Medicine and Nutrition (CTMN) in order to attempt colonization. In this regard, methods for shipping live An. darlingi to Brasilia were investigated along with the preliminary biological studies for handling, feeding and maintaining larvae

and adults. Investigations of the natural and artificial mating capabilities of these mosquitoes were studied.

In the field, experiments were conducted using mark, release and recapture methods to study the feasibility of evaluating flight behavior and dispersal of An darlingi.

PROGRESS:

1. Schistosomiasis: In FY1982 we tested 457 bottle number compounds for prophylactic (247) and/or curative (170) antischistosomal activity. Of these, 70 compounds were identified as toxic and 5 showed indications of activity requiring retest verification in the PMT. In the PCT, 23 compounds were toxic and 6 were active requiring confirmation. A total of 574 mouse test groups were utilized (including both drug test animals and control animals). Since each test group requires 5 mice, this represents a utilization of 2,870 mice. The above workload data covers the period 1 October 1980 to 11 February 1981. Four SCT procedures, testing 9 bottle number compounds, have been performed since May, 1980. These compounds were selected on the basis of prior performance in the PCT and/or PMT, and expanded the efficacy data beyond that available in the primary test systems.

In January, 1981 it became necessary to curtail drug testing because of a lack of suitable mice for use as an animal model. The reasons for this were probably combinations of health, environmental, genetic and physical facility factors. In May, 1981 the University of Brasilia initiated extensive renovations of the Central Bioterio mouse facility. Such renovations will include insolated sealed breeding and animal stock rooms, sterilization and cleaning facilities, forced air ventilation system and animal ration and bedding storage facilities. Additionally, an improved colony management program is under review. Improved waste disposal methods and sterilization of filtered mouse bedding have been implemented. In July, we received a shipment of mouse stock (random bred strain CD-1) from Charles River Breeding Laboratories via the Walter Reed Army Institute of Research. These are destined to provide the nucleus stock for rederiving the Bioterio mouse colony. In early September, production breeding was initiated with the aim of a) providing animals for drug testing and b) producing F_1 offspring for a nucleus colony. These efforts have been highly successfull and drug testing was reestablished on 26 Oct 81.

The B. glabrata snail colony is fully capable of maintaining the necessary infection level for support of the drug testing program.

However, some critical fluctuations were noted in several monitored parameters, such as percent of infection success, infected snail mortality and/or snial fecundity (egg laying sucess). Methodology and seasonal/environmental factors certainly had some influence on these fluctuations, but genetic factors may also be contributory to the situation. Considering that both the parasite and the snail were established in the laboratory from wild stock in 1973-74, we returned to the same locale (Paulista, Pernambuco) in April, 1981 and collected uninfected 514 B. glabrata snails for separate laboratory rearing. All snails were returned to the Brasilia laboratory and, during 3 generations of rearing, were evaluated against the older laboratory strain for growth and susceptibility to schistosome infection. Surprisingly, the wild snails demonstrated a slower growth rate and a lower susceptibility to infection than their lab-reared counterparts and we have rejected their possibility for laboratory life cycle maintenance.

Several programs of physical renovations were accomplished in the schistosomiasis laboratory between January 1981 and the present. A new fume hood was installed in the Pharmacy. An isolation/ weighing room was also constructed. Engineering renovations were accomplished in the animal room to improve its isolation against feral pest penetration. The entire laboratory was repainted following severe fungal infestations during the rainy season. Equipment maintenance and repair was also a priority concern during this period.

2. Malaria: Mosquito studies were conducted at the Ituxi study area during the months of March-April and June-July, 1981.

Experiments of the March-April period reconfirmed the presence of behavioral resistance of An. darlingi to year-old DDT treated paper surfaces which lined an excito-repellency chamber. Mosquito adults were also exposed to year-old DDT treated wall surfaces of the experimental house. These mosquitoes were killed within 24 hours of exposure, whereas, less than 20% of the mosquitoes had died in the control house. Marked mosquitoes, which were released in treated and control houses, left the treated house faster than the control house. We are uncertain whether the mosquitoes which left the treated house were exposed to a lethal dose of insecticide. Again, bimodal mosquito biting activity was observed during biting collections made outside of the house. Adult collections made inside of the houses were inconclusive with regards to identifying peak feeding activity since population numbers of An. darlingi were low and may have contributed to incomplete data bases. Adults, first instar larvae and eggs of An. darlingi were successfully transported to the CTMN. Methods for handling, rearing and forced mating were attempted. Yeast, yeast and mouse laboratory chow, Cerophyll®, and wheat germ were tested as food for the larvae. With

50 or less larvae per pan (12 X 7 X 2 inches), wheat germ gave the best results. Efforts toward potential colonization are encouraging, but they were unsuccessful in producing a colony on the first attempt.

The second trip, June - July, 1981, was made to replace the roofs on two experimental houses, to conduct some preliminary experiments on releasing marked mosquitoes at various distances from the study area, and to continue efforts to colonize An. darlingi. During the time the roofs were being replaced 530 mosquitoes, each marked with one of seven different colors, were released at distances of 65 meters, 120 meters and 1 kilometer from the study area. Fifty-nine of the marked specimens (representing all 7 colors) were recovered during biting collections at the study area. About 3,000 eggs, larvae and adults were returned to the CTMN and successfully reared early instars resulted in about 400 adults (1:1 males to females). After examination of 20 empty female spermathecae forced copulation techniques were tried. Even though three different kinds of anesthetizing gases were tried on blood engorged and unengorged female mosquitoes, neither decapitated male mosquitoes nor normal males could successfully inseminate the females. The process of male genitalia interlocking with the female genitalia appeared normal (3-30 seconds). The cause for the lack of spermatozoan transfer is not known. An insectary, which is near completion at the CTMN, will be used to further study the complexities of colonizing this mosquito.

RECOMENDATIONS:

1. Reimplement antischistosomal drug testing with the establishment of a new mouse production colony. Place increased emphasis on secondary curative testing.

2. Continue studies to describe the behavioral morphological and physiological characteristics of selected anopheline species, particulary An. darlingi. Conduct comparative studies in various areas of the Amazon Basin.

3. Colonize An. darlingi for vector competence, behavioral and physiological studies under laboratory conditions.

4. Continue to monitor the effectiveness of house treatment with DDT or other insecticides on malaria vectors.

5. Begin preparations for studies on falciparum malaria strain distributions and immunologic specificities in the Amazon River basin.

PRESENTATIONS:

1. Bosworth, A. and Aire Barros. 1981. Entomological hazards in tropical medicine. VI Curso de Aperfeiçoamento em Medicina. 1 Sep 81 - 24 Oct 81, Faculty of Medicine, University of Brasilia.

2. Bosworth, A. 1981. Entomology laboratory for physicians, IBID.

3. Reid, W.A. 1981. Experimental Schistosomaisis. IBID.

BIBLIOGRAPHY:

1. Bosworth, A. J. K. Olson and S. M. Meola. 1981. A study of the chorion of the egg of Psorophora columbiae. I. Taxonomic considerations. Submitted for publication to Mosquito Systematics.

2. Marsden, P. and W. Reid. 1981. New Transactions resists predations of the American conckrouch (Periplaneta americana). Transaction of the Royal Society of Tropical Medicine and Hygiene. 75:132.

3. Peterson, N.E. and R. H. Pine. 1981. Chave para identificar os mamíferos da região amazônica brasileira com exceção dos quirópteros e primatas. Submitted for publication to Acta Amazônica.

4. Peterson, N.E., Roberts, D.R., Llewellyn, C.H. and F.P. Pinheiro. 1981. Programa multidisciplinario de vigilancia de las enfermedades infecciosas en zonas colindantes con la Carretera Transamazonica en Brasil. I. Ecologia de la Region. Bulletin of the Pan American Health Organization. 91:137-148.

5. Prata, A. R., W. A. Reid, and M. S. L. Cunha. 1981. Tratamento da giardose com Tinidazol. Clínica Terapêutica.

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